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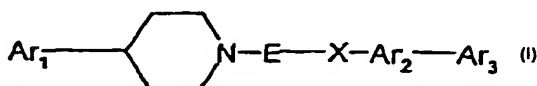
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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
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(54) Title: ARYL PIPERIDINE DERIVATIVES AS INDUCERS OF LDL-RECEPTOR EXPRESSION FOR THE TREATMENT
OF HYPERCHOLESTEROLEMIA



novel aromatic piperidines of formula (I) and their use in therapy.

(57) Abstract: This invention relates to novel compounds which
up-regulate LDL receptor (LDL-r) expression and to processes for
their preparation, pharmaceutical compositions containing them
and their medical use. More particularly, this invention relates to

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 03/07612

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/445 A61P3/06 C07D401/04 C07D417/12 C07D417/14 C07D211/14 C07D401/12 C07D413/12 C07D409/12 C07D405/12 C07D409/14		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D A61K A61P		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FORBES I T ET AL: "CCR2B receptor antagonists: conversion of a weak HTS hit to a potent lead compound" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 10, no. 16, 21 August 2000 (2000-08-21), pages 1803-1806, XP004216003 ISSN: 0960-894X example 3	1-3,5-8, 17,19
X	US 6 048 900 A (CONNELL RICHARD D ET AL) 11 April 2000 (2000-04-11) claim 1; examples 259,267,275 --- -/---	1,6,8,9, 17-19
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		
<input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : *A* document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *A* document member of the same patent family		
Date of the actual completion of the international search 14 October 2003		Date of mailing of the international search report 24/10/2003
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Johnson, C

INTERNATIONAL SEARCH REPORT

International Application No.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01 06261 A (ISSANDOU MARC ; GRAND PERRET THIERRY ANDRE REG (FR); GLAXO GROUP LT) 25 January 2001 (2001-01-25) cited in the application examples 1,2	1-19
P,X	WO 02 055495 A (BOMBRUN AGNES ; BOUILLOT ANNE MARIE JEANNE (FR); DUMAITRE BERNARD A) 18 July 2002 (2002-07-18) claim 1	1-19
P,X	WO 02 055496 A (BOMBRUN AGNES ; BOUILLOT ANNE MARIE JEANNE (FR); DUMAITRE BERNARD A) 18 July 2002 (2002-07-18) examples, e.g. ex. 15 claim 1	1-19
P,X	WO 02 055497 A (BOMBRUN AGNES ; BOUILLOT ANNE MARIE JEANNE (FR); DUMAITRE BERNARD A) 18 July 2002 (2002-07-18) examples, e.g. ex. 1 claim 1	1-19
P,X	WO 02 066469 A (HEMMERLE HORST ; URMANN MATTHIAS (DE); BORDEAU KENNETH J (US); NIED) 29 August 2002 (2002-08-29) ex. 816208, p.234 claim 1	1,5,6,8, 17,19

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/07612

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1 (part)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1 (part)

Present claim 1 relates to a compound defined by reference to a desirable characteristic or property, namely prodrugs. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. It is further noted that in the description (p. 14) prodrugs are defined as being modified derivatives of the compounds of structure (I) in which the modified functional group is cleaved either by routine manipulation or in vivo. It is unclear what is meant by routine manipulation. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds of formula (I) and their derivatives in which hydroxy, sulfhydryl and amine groups are derivatized by acetate, formate and benzoate groups and in which carboxylic acid groups are esterified (p. 15, first paragraph).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/EP 03/07612

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6048900	A	11-04-2000	US 6410792 B1	25-06-2002
WO 0106261	A	25-01-2001	AU 5984700 A	05-02-2001
			WO 0106261 A2	25-01-2001
			EP 1196783 A2	17-04-2002
			JP 2003504644 T	04-02-2003
WO 02055495	A	18-07-2002	WO 02055495 A1	18-07-2002
WO 02055496	A	18-07-2002	WO 02055496 A1	18-07-2002
WO 02055497	A	18-07-2002	WO 02055497 A1	18-07-2002
WO 02066469	A	29-08-2002	WO 02066469 A2	29-08-2002

Form PCT/ISA/210 (patent family annex) (July 1992)

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